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EXAMINER	
THOMAS, DAVID C	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/763,597	DEBOER ET AL.	
	Examiner	Art Unit	
	David C. Thomas	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *28-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 21, 2007 has been entered. Claims 1, 9, 26, 27 and 32 (currently amended) and claims 2-8 and 10-25 (original) will be examined on the merits. Claims 28-31 were previously withdrawn.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 2, 4-8 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Richter et al. (Advanced Materials (2000) 12:507-510) in view of Gertner et al. (U.S. Patent Pub. No. 2003/0060873).

With regard to claims 1, 6, 7 and 26, Richter teaches a method for metallizing one or more sites of a nucleic acid molecule (for overview, see page 508, column 1, line 54 to column 2, line 6) comprising:

providing palladium ions (Pd acetate solution was prepared, page 510, column 1, lines 1-6); and

contacting the palladium ions and a nucleic acid molecule under conditions effective to bind the palladium ions on one or more sites of the nucleic acid molecule (Pd acetate solution was mixed with a DNA solution for 2 hours, followed by a reduction step, page 510, column 1, lines 6-16; alternatively, metallization of immobilized DNA was performed by placement of a Pd solution on the DNA, followed by a reduction solution and removal of all liquids by filter paper, page 510, column 1, lines 17-28), wherein the palladium ions more strongly associate with the nucleic acid molecule than with other sites, to prevent general and spontaneous deposition of the palladium ions on sites other than the nucleic acid molecule (this is an inherent property of the compound, as evidenced by the metallization of DNA molecules in the presence of palladium acetate wherein only the DNA molecule and not a glass surface to which the DNA is

attached becomes metallized following reduction and removal of all liquids, see Richter, p. 509, column 1, lines 21-33 and Figure 3; also, see MPEP 2112-III, which states:

"Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." In re Best, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims.").

With regard to claim 2, Richter teaches a method wherein the nucleic acid molecule is DNA (p. 508, column 1, line 54 to column 2, line 6).

With regard to claim 4, Richter teaches a method wherein the palladium ions are in an aqueous solution of palladium ions (palladium used of DNA metallization is in the form of solution of palladium acetate, page 510, column 1, lines 1-6).

With regard to claim 5, Richter teaches a method wherein said contacting the palladium ions and a nucleic acid molecule is carried out for about 1 second to about 1 hour (Pd acetate is mixed with DNA solution for 2 hours, p. 510, column 1, lines 6-8).

With regard to claim 8, Richter teaches a method further comprising:

washing away excess palladium ions from the nucleic acid molecule (excess palladium ions are removed by dilution in a reduction bath and distilled water or by removal of excess liquids with filter paper, p. 510, column 1, lines 9-29).

Richter does not teach a method for metallizing a nucleic acid using a solution comprising palladium chloride that is contacted with the nucleic acid for about 1 second to about 1 hour. Richter also does not teach a method of contacting the nucleic acid having palladium ions bound with nickel or nickel allow under conditions effective to deposit nickel or nickel alloy on the nucleic acid molecule. Richter also does not teach a method of metallizing a nucleic acid by providing stannous ions and contacting the molecule having stannous ions with silver to effectively deposit silver on the nucleic acid molecule.

With regard to claim 1, Gertner teaches a metallizing method of contacting a nucleic acid molecule such as DNA (paragraph 88, lines 10-14) having palladium ions bound to one or more of its sites with nickel or nickel alloy under conditions effective to deposit nickel or nickel alloy on the nucleic acid molecule (after rinsing away palladium solution, substrate is ready for electroless deposition in aqueous solution containing nickel ions or a nickel alloy, paragraph 59, lines 1-8, paragraph 60, lines 1-7, paragraph 62, lines 1-8, and Figure 5, step 44).

With regard to claim 4, Gertner teaches a metallizing method wherein the palladium ions are in an aqueous solution of palladium chloride (palladium catalyst is deposited on surface of the substrate in form of solution of palladium chloride, paragraph 100, lines 9-14).

With regard to claims 5 and 7, Gertner teaches a metallizing method wherein said contacting the palladium ions and nickel or nickel alloy and a nucleic acid molecule

is carried out for about 1 second to about 1 hour (after palladium catalyst is deposited on substrate, substrates were placed in electroless plating baths for 10 minutes, paragraph 102, lines 4-8).

With regard to claim 6, Gertner teaches a method wherein the nickel or nickel alloy is an electroless nickel plating solution (after rinsing away palladium solution, substrate is ready for electroless deposition or plating in aqueous solution containing nickel ions or a nickel alloy, paragraph 59, lines 1-8, paragraph 60, lines 1-7, paragraph 62, lines 1-8, and Figure 5, step 44).

With regard to claim 8, Gertner teaches a method further comprising:

washing away excess palladium ions from the nucleic acid molecule prior to said contacting the nucleic acid molecule having palladium ions bound to one or more of its sites with nickel or nickel alloy (surface of substrate is rinsed with distilled water to wash away palladium solution prior to electroless plating, paragraph 100, lines 10-15).

Claim 26 is rejected under 35 U.S.C. 102(a) as being anticipated by Gertner et al. (U.S. Patent Pub. No. 2003/0060873).

With regard to claim 26, Gertner teaches a method for metallizing one or more sites of a nucleic acid molecule comprising:

providing stannous ions (metals such as Sn (tin) can be used as sensitizing agents, paragraph 45, lines 3-7);

contacting the stannous ions and a nucleic acid molecule under conditions effective to bind stannous ions on one or more sites of the nucleic acid molecule (substrate may be sensitized with stannous ions prior to performing electroless

deposition process, paragraph 45, lines 3-7), wherein the stannous ions more strongly associate with the nucleic acid molecule than with other sites, to prevent general and spontaneous deposition of the stannous ions on sites other than the nucleic acid molecule (this is an inherent property of the compound, as evidenced by electroless deposition or metals wherein other metals such as Sn (tin) in the form of stannous chloride act as sensitizing agents that would not function if the metal ions associated randomly with other surfaces, see Gertner, paragraph 45, lines 1-11 and paragraph 60, lines 1-14; also, see MPEP 2112-III, which states:

"Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." In re Best, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims.");

and

contacting the nucleic acid molecule having stannous ions bound to one or more of its sites with silver under conditions effective to deposit silver on the nucleic acid molecule (substrate can also be catalyzed with silver prior to performing electroless deposition process, paragraph 45, lines 3-8 and paragraph 64, lines 1-8).

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine the methods of Richter and Gertner for

metallizing a nucleic acid since the methods of Richter provide a means for specifically activating a DNA molecule with metals such as palladium ions which can then be treated by the methods of Gertner for electroless plating with metals such as nickel or nickel alloy. Thus, an ordinary practitioner would have been motivated to use methods of metallizing DNA with metals such as palladium as taught by Richter combined with the methods for depositing metals or metal alloys such as nickel on metallized nucleic acids using an electroless deposition method as taught by Gertner, since these methods provide an economical and scaleable approach to forming metal/bioactive structure complexes that do not damage the bioactive material in the process of deposition, since the conditions are mild, occurring at room temperature and near physiological pH, and are very controllable for a person of ordinary skill in the art (Gertner, paragraph 68, lines 5-22). Furthermore, the methods of Richter and Gertner are versatile, wherein a variety of metal ions such as palladium and tin can be used to sensitize the DNA or act as a catalyst for for deposition of a variety of metal particles such as nickel, silver, or gold (Gertner, paragraph 44, lines 1-10, paragraph 45, lines 1-11 and paragraph 64, lines 1-13). Finally, the methods of Richter and Gertner provide a means to form nanowires through metallization of immobilized DNA molecules, which can be fixed between electrical contacts on devices for purposes of detection (Richter, p. 509, column 1, lines 29-33).

5. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Richter et al. (Advanced Materials (2000) 12:507-510) in view of Gertner et al. (U.S. Patent Pub. No. 2003/0060873) and further in view of Tu et al. (U.S. Patent No. 5,945,527).

Richter and Gertner together teach the limitations of claims 1, 2, 4-8 and 26 as discussed above.

Neither Richter nor Gertner teach a method wherein the palladium ions are in a solution comprising palladium acetate, acetone, and water.

Tu teaches methods of modifying nucleosides or nucleic acids with bioagents using palladium-catalyzed reactions using palladium acetate in a solvent comprising water, ethyl acetate, and acetone (column 3, line 50 column 4, lines 15, column 8, lines 54-67, and claim 17).

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine the methods of Richter and Gertner with that of Tu to modify nucleic acids by modifying bases on the nucleic acid with nickel or nickel alloys using the solution taught by Tu comprising a palladium catalyst, water, ethyl acetate, and acetone, along with a suitable nucleophile to attach to the nucleic acid. Thus, an ordinary practitioner would have been motivated to use such a solvent to modify the nucleic acids since the methods of Tu are versatile and can modify both pyrimidine and purine nucleosides at a variety of positions (Tu, column 1, lines 9-14 and claim 17), to produce labeled nucleic acids and oligonucleotides suitable for a variety of biological uses (Tu, column 1, lines 15-19 and column 4, lines 8-15).

6. Claims 9, 10, 12-25 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fish (U.S. Patent Pub. No. 2004/0132220) in view of Richter et al. (Advanced Materials (2000) 12:507-510) and further in view of Gertner et al. (U.S. Patent Pub. No. 2003/0060873).

With regard to claims 9, 12 and 16-19, Fish teaches a method for detecting a target nucleic acid molecule in a sample comprising:

providing a device for detecting the presence of a target nucleic acid molecule in a sample (for overview, see paragraph 15, lines 1-13) comprising:

two electrical conductors, including a first electrical conductor and a second electrical conductor, wherein the electrical conductors are not in contact with one another (two electrodes of opposite polarity are in close proximity but are prevented from direct contact, paragraph 17, lines 4-18 and paragraph 21, lines 19-26); and

one or more sets of two oligonucleotide probes attached to the electrical conductors, wherein the probes are positioned such that they cannot come into contact with one another (probes, or binding agents, are attached to surface of electrodes, paragraph 92, lines 11-13, paragraph 160, lines 1-4 and Figure 2C, parts 16 and 16a) and such that a target nucleic acid molecule, which has two sequences, a first sequence complementary to a first probe attached to the first electrical conductor and a second sequence complementary to a second probe attached to the second electrical conductor, can bind to both probes (two molecules of analyte, parts 15a and b, each bind to each probe at different ends of the sequence, parts 16a and b, as well as to

sequence on ends of nanotube, to form bridge between electrodes, paragraph 92, lines 11-16 and Figure 2C and D);

contacting the probes with a sample which may have the target nucleic acid molecule under selective hybridization conditions to permit target nucleic acid molecules (hybridization conditions are provided for optimal temperature and salt concentration, paragraph 161, lines 1-18), if any, present in the sample to hybridize to both of the probes and form a complex of the target nucleic acid molecule hybridized to the probes (two molecules of analyte, parts 15a and b, each bind to each probe at different ends of the sequence, parts 16a and b, as well as to nanotube sequence, to form bridge between electrodes, paragraph 92, lines 11-16 and Figure 2C and D);

determining if an electrical current can be carried between the probes, said electrical current between the probes indicating the presence of the target nucleic acid molecule in the sample (presence of analyte places detection circuits of electrodes in second state to provide signaling and read-outs to indicate identity and/or amount of analyte present, paragraph 88, lines 1-12).

With regard to claim 10, Fish teaches a method wherein the target nucleic acid molecule is DNA or RNA (molecules that can be detected include DNA and RNA, paragraph 19, lines 1-13).

With regard to claim 13, Fish teaches a method wherein the sample is whole blood or peripheral blood lymphocytes (blood is removed directly from subject into the instrument, paragraph 114, lines 1-27; blood cells include T&NK cells, T helper cells, T cells, and suppressor cells, paragraph 168, lines 6-10).

With regard to claim 14, Fish teaches a method wherein said method is used to detect infectious agents (such as *E. coli* bacteria and other infectious agents, paragraph 14, lines 4-13, paragraph 114, lines 33-35 and paragraph 168, lines 10-11).

With regard to claim 15, Fish teaches a method wherein said method is used for nucleic acid sequencing (such as single-base sequencing for SNP applications, paragraph 159, lines 10-20).

With regard to claim 20, Fish teaches a method wherein the probes are complementary to sequences from the genetic material of a pathogenic bacteria (DNA of pathogens can be detected, paragraph 168, lines 1-11).

With regard to claim 21, Fish teaches a method wherein the pathogenic bacteria is a biowarfare agent (methods can be used for anti-terrorist purposes, paragraph 14, lines 13-16).

With regard to claim 22, Fish teaches a method wherein the pathogenic bacteria is a food borne pathogen (method can be used for food and water safety measurements, paragraph 14, lines 13-15).

With regard to claim 23, Fish teaches a method wherein the probes are complementary to sequences from the genetic material of a virus (methods include assays for various viral agents such as HIV, hepatitis viruses, adenovirus, and influenza viruses, paragraph 157, lines 29-31).

With regard to claim 24, Fish teaches a method wherein the probes are complementary to sequences from the genetic material of a human (methods are used

in DNA diagnostics for human, as well as other animal and plant samples, paragraph 159, lines 20-25).

With regard to claim 25, Fish teaches a method wherein one or both of the probes has a sequence which is complementary to a sequence having a polymorphism, wherein the base or bases complementary to the polymorphism are located at an end of the probe distal to the conductors (method can be used to detect single nucleotide polymorphisms (SNPs), paragraph 159, lines 10-20; PCR or ligase chain reaction assays can be used for detecting specific sequences with the device, paragraph 162, lines 1-7).

With regard to claim 27, Fish teaches a method for detecting a target nucleic acid molecule in a sample comprising:

providing a device for detecting the presence of a target nucleic acid molecule in a sample (for overview, see paragraph 15, lines 1-13) comprising:

two electrical conductors, including a first electrical conductor and a second electrical conductor, wherein the electrical conductors are not in contact with one another (two electrodes of opposite polarity are in close proximity but are prevented from direct contact, paragraph 17, lines 4-18 and paragraph 21, lines 19-26); and

one or more sets of two oligonucleotide probes attached to the electrical conductors, wherein the probes are positioned such that they cannot come into contact with one another (probes, or binding agents, are attached to surface of electrodes, paragraph 92, lines 11-13, paragraph 160, lines 1-4 and Figure 2C, parts 16 and 16a) and such that a target nucleic acid molecule, which has two sequences, a first

sequence complementary to a first probe attached to the first electrical conductor and a second sequence complementary to a second probe attached to the second electrical conductor, can bind to both probes (two molecules of analyte, parts 15a and b, each bind to each probe at different ends of the sequence, parts 16a and b, as well as to sequence on ends of nanotube, to form bridge between electrodes, paragraph 92, lines 11-16 and Figure 2C and D);

contacting the probes with a sample which may have the target nucleic acid molecule under selective hybridization conditions to permit target nucleic acid molecules (hybridization conditions are provided for optimal temperature and salt concentration, paragraph 161, lines 1-18), if any, present in the sample to hybridize to both of the probes and form a complex of the target nucleic acid molecule hybridized to the probes (two molecules of analyte, parts 15a and b, each bind to each probe at different ends of the sequence, parts 16a and b, as well as to nanotube sequence, to form bridge between electrodes, paragraph 92, lines 11-16 and Figure 2C and D); and

determining if an electrical current can be carried between the probes, said electrical current between the probes indicating the presence of the target nucleic acid molecule in the sample (presence of analyte places detection circuits of electrodes in second state to provide signaling and read-outs to indicate identity and/or amount of analyte present, paragraph 88, lines 1-12).

Fish does not teach a method of providing palladium ions, such as in an aqueous solution of palladium chloride, and contacting the palladium ions with the device after said contacting the probes with the sample under conditions effective to bind the

palladium ions on one or more sites of any of the complex of the target nucleic acid molecules hybridized to the probes. Fish also does not teach a method of contacting the device with nickel or nickel alloy, wherein said contacting the device with nickel is carried out for about 1 second to about 1 hour, under conditions effective to deposit nickel or nickel alloy on the complex, after washing away excess palladium ions. Fish also does not teach a method of providing stannous ions, contacting the stannous ions with the device after said contacting the probes with the sample under conditions effective to bind the stannous ions on one or more sites of any of the complex of the target nucleic acid molecules hybridized to the probes, and contacting the device with silver under conditions effective to deposit silver on the complex of the nucleic acid molecules hybridized to the probes.

Richter teaches a method of providing palladium ions (such as Pd acetate solution, page 510, column 1, lines 1-6) and contacting the palladium ions and a nucleic acid molecule under conditions effective to bind the palladium ions on one or more sites of the target nucleic acid molecules hybridized to a probe (Pd acetate solution was mixed with a DNA solution for 2 hours, followed by a reduction step, page 510, column 1, lines 6-16; alternatively, metallization of immobilized DNA was performed by placement of a Pd solution on the DNA, followed by a reduction solution and removal of all liquids by filter paper, page 510, column 1, lines 17-28; lambda DNA, p. 510, column 1, lines 6-8, is double-stranded, as would be a probe interaction with a target nucleic acid).

With regard to the limitation: "wherein the palladium or stannous ions more strongly associate with the nucleic acid molecule than with other sites, to prevent general and spontaneous deposition of the palladium ions on sites other than the nucleic acid molecule", this is an inherent property of these compounds, as evidenced by metallization of DNA molecules in the presence of palladium acetate wherein only the DNA molecule and not a glass surface to which the DNA is attached becomes metallized following reduction and removal of all liquids, see Richter, p. 509, column 1, lines 21-33 and Figure 3 and also evidenced by electroless deposition or metals wherein other metals such as Sn (tin) in the form of stannous chloride act as sensitizing agents that would not function if the metal ions associated randomly with other surfaces, see Gertner, paragraph 45, lines 1-11 and paragraph 60, lines 1-14; also, see MPEP 2112-III, which states:

"Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." In re Best, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims.").

Gertner teaches a method of contacting the device with nickel or nickel alloy under conditions effective to deposit nickel or nickel alloy on the complex after washing

away excess palladium ions (after rinsing away palladium solution, substrate is ready for electroless deposition or plating in aqueous solution containing nickel ions or a nickel alloy, paragraph 59, lines 1-8, paragraph 60, lines 1-7, paragraph 62, lines 1-8, and Figure 5, step 44). Gertner also teaches a method for metallizing one or more sites of a nucleic acid molecule comprising providing stannous ions (metals such as Sn (tin) can be used as sensitizing agents, paragraph 45, lines 3-7), contacting the stannous ions and a nucleic acid molecule under conditions effective to bind stannous ions on one or more sites of the nucleic acid molecule (substrate may be sensitized with stannous ions prior to performing electroless deposition process, paragraph 45, lines 3-7); and contacting the nucleic acid molecule having stannous ions bound to one or more of its sites with silver under conditions effective to deposit silver on the nucleic acid molecule (substrate can also be catalyzed with silver prior to performing electroless deposition process, paragraph 45, lines 3-8 and paragraph 64, lines 1-8).

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine the methods of Fish for detecting a target molecule in a sample and the methods of Richter and Gertner for metallizing a nucleic acid such as a probe or target molecule since the methods of Richter and Gertner enable detection of the nucleic acid probe/target complex when the target is hybridized to two probes in the methods of the device taught by Fish. Thus, an ordinary practitioner would have been motivated to use methods of metallizing DNA with palladium as taught by Richter combined with the methods for depositing metals or metal alloys such as nickel on metallized nucleic acids using an electroless deposition

method as taught by Gertner, since these methods provide an economical and scaleable approach to forming metal/bioactive structure complexes that do not damage the bioactive material in the process of deposition, since the conditions are mild, occurring at room temperature and near physiological pH, and are very controllable for a person of ordinary skill in the art (Gertner, paragraph 68, lines 5-22). Furthermore, the methods of Richter and Gertner are versatile, wherein a variety of metal ions such as palladium and tin can be used to sensitize the DNA or act as a catalyst for for deposition of a variety of metal particles such as nickel, silver, or gold (Gertner, paragraph 44, lines 1-10, paragraph 45, lines 1-11 and paragraph 64, lines 1-13).

7. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fish (U.S. Patent Pub. No. 2004/0132220) in view of Richter et al. (Advanced Materials (2000) 12:507-510) and further in view of Gertner et al. (U.S. Patent Pub. No. 2003/0060873) and further in view of Tu et al. (U.S. Patent No. 5,945,527).

Fish, Richter and Gertner together teach the limitations of claims 9, 10, 12-25 and 27 as discussed above.

Fish and Gertner do not teach a method wherein the palladium ions are in a solution comprising palladium acetate, acetone, and water.

Tu teaches methods of modifying nucleosides or nucleic acids with bioagents using palladium-catalyzed reactions using palladium acetate in a solvent comprising water, ethyl acetate and acetone (column 3, line 50 column 4, lines 15, column 8, lines 54-67, and claim 17).

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine the methods of Fish, Richter, Gertner and Tu to modify nucleic acids by modifying bases on the nucleic acid with nickel or nickel alloys using the solution taught by Tu comprising a palladium catalyst, water, ethyl acetate, and acetone, along with a suitable nucleophile to attach to the nucleic acid. Thus, an ordinary practitioner would have been motivated to use such a solvent to modify the nucleic acids since the methods of Tu are versatile and can modify both pyrimidine and purine nucleosides at a variety of positions (Tu, column 1, lines 9-14 and claim 17), to produce labeled nucleic acids and oligonucleotides suitable for a variety of biological uses (Tu, column 1, lines 15-19 and column 4, lines 8-15). Such modified nucleic acids would be readily useable in the device of Fish since the modification occurs after the nucleic acid is bound to capture probes attached to the electrodes, and would thus not interfere with hybridization (Fish, Figure 2C and D).

8. Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fish (U.S. Patent Pub. No. 2004/0132220) in view of Zocchi et al. (U.S. Patent Pub. No. 2004/0241699) as evidenced by Richter et al. (Advanced Materials (2000) 12:507-510).

With regard to claim 32, Fish teaches a method for detecting a target nucleic acid molecule in a sample comprising:

providing a device for detecting the presence of a target nucleic acid molecule in a sample comprising (for overview, see paragraph 15, lines 1-13):

two electrical conductors, including a first electrical conductor and a second electrical conductor, wherein the electrical conductors are not in contact with one

another (two electrodes of opposite polarity are in close proximity but are prevented from direct contact, paragraph 17, lines 4-18 and paragraph 21, lines 19-26); and

one or more sets of two oligonucleotide probes attached to the electrical conductors, wherein the probes are positioned such that they cannot come into contact with one another (probes, or binding agents, are attached to surface of electrodes, paragraph 92, lines 11-13, paragraph 160, lines 1-4 and Figure 2C, parts 16 and 16a) and such that a target nucleic acid molecule, which has two sequences, a first sequence complementary to a first probe attached to the first electrical conductor and a second sequence complementary to a second probe attached to the second electrical conductor, can bind to both probes (two molecules of analyte, parts 15a and b, each bind to each probe at different ends of the sequence, parts 16a and b, as well as to sequence on ends of nanotube, to form bridge between electrodes, paragraph 92, lines 11-16 and Figure 2C and D);

contacting the probes with a sample which may have the target nucleic acid molecule under selective hybridization conditions to permit target nucleic acid molecules (hybridization conditions are provided for optimal temperature and salt concentration, paragraph 161, lines 1-18), if any, present in the sample to hybridize to both of the probes and form a complex of the target nucleic acid molecule hybridized to the probes (two molecules of analyte in Figures 2C and D, parts 15a and b, each bind to each probe at different ends of the sequence, parts 16a and b, as well as to nanotube sequence, to form bridge between electrodes, paragraph 92, lines 11-16 and Figure 2C and D);

attaching to the probes and any target nucleic acid molecule metal ions (such as electrically readable particles, which can include gold (paragraph 121, lines 1-17), wherein the metal ions more strongly associate with the nucleic acid molecule than with other sites, to prevent general and spontaneous deposition of the metal ions on sites other than the nucleic acid molecule (this is an inherent property of the certain metal compounds, as evidenced by metallization of DNA molecules in the presence of palladium acetate wherein only the DNA molecule and not a glass surface to which the DNA is attached becomes metallized following reduction and removal of all liquids, see Richter, p. 509, column 1, lines 21-33 and Figure 3; also, see MPEP 2112-III, which states:

"Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." In re Best, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims.");

and

determining the presence of the target nucleic acid molecule in the sample (presence of analyte places detection circuits of electrodes in second state to provide signaling and read-outs to indicate identity and/or amount of analyte present, paragraph 88, lines 1-12).

Fish does not teach a method of determining the presence of the target nucleic acid molecule in the sample by detecting the scatter of light caused by the metal ions attached to the probes and any target nucleic acid molecule.

Zocchi teaches a method of detecting polynucleotide hybridization using light scattering particles bound to the polynucleotide probe, including metal particles and colloidal metals such as colloidal gold (paragraph 41, lines 1-24).

It would have been prima facie obvious to one having ordinary skill in the art at the time the invention was made to combine the methods of Fish for detecting a target molecule in a sample and Zocchi to detect polynucleotide hybridization since Zocchi teaches a highly sensitive method of detecting probe and target molecule hybridization using metal particles that scatter light to provide an alternative method for the detection system of Fish. Thus, an ordinary practitioner would have been motivated to use a light scattering detection system in the methods of Fish since this method is capable of detecting single target molecules with enhanced discrimination and eliminates the need to directly label the target, such as with fluorescent markers (Zocchi, paragraph 36, lines 1-19), thus providing a versatile assay and the means for more cost-effective devices (Zocchi, paragraph 35, lines 5-11). Furthermore, the methods of Zocchi is easily adaptable to the methods of Fish since probes can be linked to a solid surface such as a conductor or array matrix at one end and marked at the free end with a scatterer such as a metal particle (Zocchi, paragraph 41, lines 1-11).

Response to Arguments

9. Applicant's arguments filed September 21, 2007 have been fully considered but they are not persuasive.

Applicant argues that the rejection of claims 1, 2, 4-8 and 26 under 35 U.S.C. § 102(e) as being anticipated by Gertner et al. (U.S. Patent Pub. No. 2003/0060873) should be withdrawn since the reference does not teach or disclose all the limitations of the claims as amended. In particular, Applicant argues that the metal ions of the instant invention strongly associate with the nucleic acid to prevent general and spontaneous deposition of the metal ions on sites other than the nucleic acid molecule. Furthermore. Applicant argues that Gertner does not teach a method of plating metal exclusively onto a nucleic acid molecule but rather an entire substrate such as a surrounding solid surface, which is coated with a metal/nucleic acid co-deposition. The Examiner asserts that the palladium ions of the instant invention (or stannous ions) have inherent properties identical to the same compositions found in the prior art and therefore the palladium ions taught by Gertner would also preferentially bind to nucleic acids. However, the Examiner agrees that Gertner does not teach metallization of primarily a DNA molecule, but rather a bioactive complex that includes nucleic acids on a substrate. Therefore, the 102(a) rejection is withdrawn.

However, upon further searching, a new reference was found (Richter et al., Advanced Materials (2000) 12:507-510) that teaches methods of metallizing a DNA molecule with a palladium solution without coating the surrounding surfaces such as a glass slide with palladium ions. This method is compatible with the electroless deposition process taught by Gertner since the palladium-treated DNA can be readily

coated with metals such as nickel or nickel alloys. Therefore, claims 1, 2, 4-8 and 26 are now rejected under 35 U.S.C. § 103(a) as being unpatentable over Richter in view of Gertner.

Applicant then argues that the rejection of claim 3 under 35 U.S.C. § 103(a) as being unpatentable over Gertner in view of Tu et al. (U.S. Patent No. 5,945,527) should be withdrawn since neither reference teaches or discloses the limitations of the claim as amended. As discussed above, claims 1, 2, 4-8 and 26 are now rejected under 35 U.S.C. § 103(a) as being unpatentable over Richter in view of Gertner. Since Tu teaches the additional limitations of dependent claim 3, this claim is now rejected under 103(a) over Richter in view of Gertner and further in view of Tu.

Applicant then argues that the rejection of claims 9, 10, 12-25 and 27 under 35 U.S.C. § 103(a) as being unpatentable over Fish (U.S. Patent Pub. No. 2004/0132220) in view of Gertner should be withdrawn since neither reference teaches or discloses all the limitations of the claims as amended. In particular, Applicant argues that use of the methods of Gertner would short out the sensors in the electrode system of Fish. As discussed above, claims 1, 2, 4-8 and 26 are now rejected under 35 U.S.C. § 103(a) as being unpatentable over Richter in view of Gertner since Richter teaches methods for metallizing a DNA molecule without coating surrounding surfaces. Therefore, the methods of Richter are compatible in the device of Fish and would not short out the sensors. Richter also suggests that DNA metallized with palladium can be used in devices wherein the DNA is fixed between electrical contacts (Richter, p. 509, column 1, lines 29-33). Furthermore, the metallizing methods of Richter can also be used with the

methods of Gertner for electroless deposition of nickel or nickel alloys on palladium-treated DNA or deposition of silver on tin-treated DNA. Thus, claims 9, 10, 12-25 and 27 are now rejected under 35 U.S.C. § 103(a) as being unpatentable over Fish in view of Richter and further in view of Gertner.

Applicant then argues that the rejection of claim 11 under 35 U.S.C. § 103(a) as being unpatentable over Fish in view of Gertner and further in view of Tu should be withdrawn since none of the references teach or disclose the limitations of the claim as amended. As discussed above, claims 9, 10, 12-25 and 27 are now rejected under 35 U.S.C. § 103(a) as being unpatentable over Fish in view of Richter and further in view of Gertner. Therefore, Since Tu teaches the additional limitations of dependent claim 11, this claim is now rejected under 103(a) over Fish in view of Richter and further in view of Gertner and further in view of Tu.

Finally, Applicant argues that the rejection of claim 32 under 35 U.S.C. § 103(a) as being unpatentable over Fish in view of Zocchi (U.S. Patent Pub. No. 2004/0241699) should be withdrawn since the combination of the references fail to teach or disclose all the limitations of the claim as amended. As stated above, The Examiner asserts that the metal ions taught by the instant invention (such as palladium or stannous ions) have inherent properties identical to those of the same compositions found in the prior art and therefore such ions would also preferentially bind to nucleic acids without coating surrounding surfaces. This is supported by the teachings of Richter. Therefore, the 103(a) rejection of claim 32 over Fish in view of Zocchi is maintained, as evidenced by Richter.

Conclusion

10. Claims 1-27 and 32 are rejected. No claims are allowable.

Correspondence

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David C. Thomas whose telephone number is 571-272-3320 and whose fax number is 571-273-3320. The examiner can normally be reached on 5 days, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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